REMARKS

Status of the Claims

Claims 1-13 and 35-38 are pending in the present application, Claims 14-34 having been cancelled in the present amendment in response to a restriction requirement, and new Claims 35-38 having been added. Claims 1 and 5 have been amended to more clearly define the invention.

Telephone Restriction and Subsequent Election

On December 16, 2004 Examiner Levkovich advised applicants' attorney (Ronald Anderson) by telephone that the claims in the present application define two patentably distinct inventions. The Examiner noted that a first invention is defined by Claims 1 - 13, and a second invention is defined by Claims 14 - 34. The Examiner further noted that the first invention is directed to apparatus for optimizing reaction parameters, while the second invention is directed to a method for optimizing reaction parameters.

On December 17, 2004 applicants' attorney (Michael King) contacted Examiner Levkovich by telephone and provisionally elected Claims 1-13, with traverse.

In the current Office Action, the Examiner has justified the restriction by asserting that the method of Claims 14-34 can be executed by a system not incorporating the dilution pump included in Claims 1-13. Applicants hereby affirmatively confirm the election of Claims1-13, without, subject to the right to file a divisional application directed to the non-elected invention.

Rejection under 35 U.S.C. § 102

The Examiner has rejected Claims 1-8 under 35 § U.S.C. § 102 as being anticipated by Bard (U.S. 5,580,523). The Examiner asserts that Bard discloses reactor system including a processor configured to implement optimization reactions and a dilution pump for each reactant, each dilution pump being coupled in fluid communication with a corresponding reactant supply source and with a solvent supply source for the corresponding reactant, and being logically coupled to the controller and operative to vary a concentration of the corresponding reacting using a solvent. Applicants respectfully disagree for the following reasons.

While there certainly are similarities between Bard's reactor system and the present invention, there are two significant differences. First, the controller in the present invention is configured to implement functions not implemented by the controller disclosed by Bard, and second, the dilution pump implemented in the present invention is structurally distinguishable over the solvent pump

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

disclosed by Bard. Applicants have amended independent Claim 1 and added new Claim 37 to more clearly highlight these distinguishing elements.

With respect to Claim 1, it is clear that Bard's controller can be used to control elements included in Bard's reaction system, including pumps, valves and a thermal conditioning system. Bard's controller is also logically coupled to one or more detectors. Bard clearly indicates that the controller can be used to optimize control of residence time within a reaction zone (Abstract). The Examiner notes that Bard discloses that his reaction system can be monitored to regulate the reaction process and/or create an optimal environment for synthesis. Clearly, one can program Bard's controller with a set of optimal reaction conditions, and Bard's controller will monitor the reaction system to ensure that those optimal reaction conditions are met. Significantly, Bard's controller is configured to address a different need than the controller in applicants' invention is configured to meet. Specifically, Bard's controller is used to control the functioning of a reaction system according to optimal reaction parameters that are programmed into the control system. Applicants' controller is configured to perform a plurality of optimization experiments in order to determine those optimal reaction parameters. As amended, Claim 1 specifically recites that the controller is configured to implement a plurality of optimization experiments, "*wherein during each of the plurality of optimization experiments, at least one of a plurality of reaction parameters controlled by the controller is changed, the plurality of reaction parameters including at least the parameters of temperature and reactant concentration.*" As discussed in detail in applicants' specification, the controller in the present invention is configured to selectively vary a set of reaction parameters according to a predefined protocol, and to collect data corresponding to the chemical products produced under those reaction parameters. By comparing the data collected from the plurality of different optimization experiments, a set of optimal reaction parameters can be identified. Those optimal reaction parameters can then be used in Bard's reaction system to produce a chemical product under optimal conditions.

Argeundo, from a structural standpoint Bard's controller *could* be configured to continuously implement a plurality of different optimization experiments, to selectively vary a set of reaction parameters according to a predefined protocol, and to collect data corresponding to the chemical products produced under those reaction parameters. However, Bard does not teach or suggest programming or otherwise configuring a controller to implement those specific functions. Thus

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

applicants' recited controller can be structurally distinguished over the controller described by Bard, on the basis of the functions the controller is configured to implement. As noted in applicants' *Background of the Invention* section, prior art systems configured to determine optimal reaction parameters generally perform optimization experiments as a batch process, as opposed to a continuous process, or perform optimization experiments using a chemical reaction system configured to simultaneously execute a series of parallel reactions, in which a different reaction parameter is varied in each of the parallel reactions. Significantly, there is no evidence to indicate that one of ordinary skill in the art would have recognized that Bard's reaction system could be modified/programmed to implement a series of optimization experiments to identify optimal reaction parameters in a continuously running system. The cited art simply does not teach or suggest such a modification, nor is there any evidence that such a modification would solve the problem recognized in the art.

Thus Claim 1 as amended distinguishes over Bard, and each claim depending on Claim 1 is distinguished over Bard for at least the same reasons. Accordingly, the rejection of Claims 1-8 as being anticipated by Bard should be withdrawn.

Claim 5 has been amended to further recite that the predefined protocol implemented by the processor to carry out the plurality of optimization reactions comprises at least one of: "*implementing a plurality of optimization experiments in which each reaction parameter has been predefined; implementing a plurality of optimization experiments in which each reaction parameter is varied between a predefined maximum value and a predefined minimum value based on a predefined function; and implementing a plurality of optimization experiments in which each reaction parameter in an initial set of optimization experiments are predefined, and in which at least one reaction parameter in a later set of optimization experiments is determined based on results from the initial set of optimization experiments.*" Bard does not teach or suggest any equivalent predefined protocol for implementing a plurality of optimization reactions. Claim 5 is therefore distinguishable over Bard for this additional reason,

The Examiner has also rejected claims in the present application based on Dasgupta, as will be discussed in greater detail below. Even if one of ordinary skill in the art would have been motivated to modify Bard's controller based on Dasgupta's disclosure, an equivalent invention would not be achieved. Significantly, Dasgupta does not teach or suggest a controller configured to control

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

a reactor system to produce a chemical product. Dasgupta specifically refers to controlling an *analytical technique* referred to as titration. Dasgupta teaches a controller configured to control the titration process by manipulating the relative concentrations of a sample and a titrant so that the total flow in the system is constant (that is, when the flow of the titrant is increased, the flow of sample is decreased, see paragraph 14 of Dasgupta). Thus, Dasgupta teaches controlling an analytical technique using a controller configured to continuously control the concentrations and flow rates of both a sample and a titrant. Note that Claim 1 specifically recites a controller configured to control reaction parameters including *at least* temperature and reactant concentration. At best, modifying Bard's controller in view of Dasgupta would achieve a controller configured to selectively vary reactant concentrations over time. The cited art does not teach or suggest configuring a controller to selectively vary a plurality of reaction parameters while continuously performing a plurality of optimization experiments, where the plurality of reaction parameters include both temperature and reactant concentration.

Furthermore, it must be recognized that Dasgupta does not teach a controller configured to control a chemical reactor. Dasgupta is not directed to the generation of a chemical product, and there is no reason to conclude that one of ordinary skill in the art would have looked to a technique for controlling an analytical process for guidance in modifying a controller to control a system and process involved in generating a chemical product. Dasgupta ***does not*** teach or suggest techniques directed to determining optimal reaction parameters for a reaction; instead, Dasgupta teaches a controller configured to control a continuous chemical analytical process involving a sample and a titrant. Thus, there does not appear to be any motivation to combine the references in the manner suggested by the Examiner, and such a combination does not support a *prima facie* basis for rejecting applicants' claims as obvious.

Applicants further respectfully submit that Claims 4, 7, and 8 were distinguishable over Bard even before the above-noted amendment to Claim 1. Claim 4 specifically recites a controller configured to implement a particular function involving directing a flow of fluid through a plurality of residence time chambers. Merely because Bard discloses a chemical reactor that can be used in connection with a residence time chamber (or a plurality of residence time chambers) does not merit a conclusion that Bard discloses a controller that implements a function equivalent to that claimed by applicants. FIGURES 1B-1E as filed with the present application schematically illustrate the control

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

function recited in Claim 4. Significantly, neither Bard nor Dasgupta teaches or suggests an equivalent control function. Claim 4 is therefore distinguishable over the cited art for this additional reason.

Claims 7 and 8 specifically recite a controller configured to selectively control a specific reaction parameter over time while monitoring the chemical product produced using those reaction parameters, in order to determine optimal reaction parameters. Bard's system is configured to receive input from a user, so that once optimal reaction parameters have been at determined, Bard's invention implements the optimal reaction parameters and controls the reaction system to adhere to these previously determined optimal reaction parameters. Neither Bard nor Dasgupta teaches or suggests a controller configured to perform a plurality of optimization experiments by selectively varying the reaction parameters while collecting analytical data about the product produced using those reaction parameters to determine optimal reaction parameters.

<u>Rejection under 35 U.S.C. § 103</u>

The Examiner has also rejected Claims 9-13 under 35 USC § 103(a) as being unpatentable over Bard (U.S. 5,580,523) in view of Dasgupta (U.S. Patent Publication 20020151080). The Examiner asserts that Dasgupta discloses monitoring reaction parameters according to a periodic pattern and asserts that it would have been obvious to one of ordinary skill in the art at the time of the invention to have modified Bard's controller using Dasgupta's control techniques for optimizing continuously monitored parameters of an automated reaction system. Applicants respectfully disagree for the following reasons.

With respect to Bard, the Examiner appears to have concluded that Bard discloses a reaction system configured to determine optimal reaction parameters. Applicants respectfully submit that Bard does not teach or suggest any control techniques that can be used to ***determine*** optimal reaction parameters. Instead, Bard discloses a reaction system and a controller configured to ***maintain*** optimal reaction conditions. Clearly, those optimal reaction parameters must be provided to Bard's controller in order for Bard's reaction system to function. Bard does not teach or suggest a technique for actually *determining* those optimal reaction parameters. Significantly, Dasgupta also does not teach or suggest a technique for determining optimal reaction parameters. Accordingly, it is not apparent how a combination of these two references could achieve applicants' claimed invention, which as recited in Claim 1 (as amended), is directed to a system including a controller configured to

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

continuously perform *"a plurality of optimization experiments, such that during each of the plurality of optimization experiments, at least one of a plurality of reaction parameters controlled by the controller is changed according to a predefined protocol, the plurality of reaction parameters including at least the parameters of temperature and reactant concentration, the plurality of optimization experiments enabling optimal reaction parameters to be identified."*

Dasgupta teaches a technique for controlling an analytical process (titration) by selectively varying the flow of a titrant, while ensuring that the flow of the sample is simultaneously controlled to achieve a total constant flow (in particular, see paragraphs 14 and 31 of Dasgupta). It is not apparent why one of ordinary skill in the art would consider a control technique configured to control titration would be applicable to controlling a plurality of optimization experiments conducted in order to determine optimal reaction parameters to be implemented in producing a desired chemical product. Significantly, Dasgupta does not teach or suggest that the control techniques disclosed therein would have any applicability to controlling a system configured to produce a chemical product, as opposed to controlling a system configured to implement titration based analysis. There is no basis to conclude that the problems encountered in titration analysis have any relationship to the problems encountered in controlling a chemical reaction. There is no basis in the cited art for concluding that one of ordinary skill in the art at the time of the invention would have been led to modify Bard's controller in view of Dasgupta's disclosure. Thus, as discussed above, the suggested combination of Bard and Dasgupta does not support a *prima facie* for rejecting applicants' claims as obvious.

It should also be noted that in suggesting the combination of Bard and Dasgupta as supporting a rejection of applicants' claims, the Examiner has not indicated any expected benefit that would motivate one of ordinary skill in the art to make such a combination. A proper obviousness rejection must include an identification of the motivation that would lead one of ordinary skill in the art to make such combination, and that motivation does not appear to be present with respect to a proposed combination of Bard and Dasgupta.

Furthermore, even if Bard's controller were modified in view of Dasgupta, the resulting controller would only be configured to vary the concentrations of the reactants such that the total flow remains the same. As noted above, Claim 1 has been amended to specifically recite that the reaction parameters varied by the controller include *temperature and concentration*. While Bard's controller is configured to enable temperature control, there is no teaching in Bard or in Dasgupta of

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

a control technique that continuously selectively varies at least one of a plurality of parameters that includes temperature and concentration. Thus, the combination of references suggested by the Examiner does not achieve an equivalent invention. Claim 1 as amended distinguishes over the combination of Bard and Dasgupta, and each claim depending on Claim 1 is distinguished over the cited art for at least the same reasons. Accordingly, the rejection of Claim 1-13 as being obvious over Bard in view of Dasgupta should be withdrawn.

Claim 12 specifically recites that each of at least two reaction parameters *are varied by the controller according to different periodic functions.* Dasgupta teaches that while a preferred embodiment implements a linear scan rate to selectively vary the flow rate of the titrant, different scan rates, having different waveforms (including waveforms with increasing and decreasing slopes), can be employed to control the flow rate of the titrant (see paragraph 54). However, using different functions to selectively vary the flow rate of the titrant is not equivalent to varying at least two reaction parameters using different periodic functions. According to Dasgupta, both the flow rate of the titrant and the flow rate of the sample are controlled based on a single function. Whatever function is used to vary the flow rate of the titrant must also be used to determine the change in the flow rate of the sample, because as disclosed by Dasgupta, any change in the flow rate of the titrant must also result in a corresponding change in the flow rate of the sample, so that a constant flow rate is maintained (see paragraph 14). The control scheme of Dasgupta is thus not equivalent to varying at least two reaction parameters according to different periodic functions, as claimed by applicants. Claim 12 is distinguishable over the combination of Bard and Dasgupta for this additional reason.

Claim 13 also includes subject matter that goes beyond any possible combination of Bard and Dasgupta. Claim 13 specifically recites that after at least two reaction parameters have been varied according to their respective functions, the controller is configured to identify new upper and lower boundaries for those reaction parameters. The controller then redefines the periodic functions, and once again selectively varies the reaction parameters based on those redefined periodic functions. Dasgupta does not teach or suggest identifying new upper and lower boundaries for each reaction parameter and redefining the periodic function used to selectively vary that reaction parameter. Claim 13 is distinguishable over the combination of Bard and Dasgupta for this additional reason.

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LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

Patentability of Newly Added Claims

New Claims 35-38 have been added in the present amendment. These claims are fully supported by the specification and are consistent with the election made in response to the restriction requirement.

Claim 35 depends from Claim 1, and is therefore patentable for at least the same reason as Claim 1. Furthermore, Claim 35 recites that the controller is configured to use a baseline value for each reaction parameter to generate the desired product, then determine at least one of a quantity and a quality of the desired product generated using the baseline values, change the baseline value for at least one reaction parameter, thereby affecting the desired product being produced by the automated system, and then determine at least one of a quantity and a quality of the desired product generated using the at least one baseline value that was changed. As discussed above, Bard does not teach or suggest *any* technique that can be used to determine optimal reaction parameters. Dasgupta teaches controlling an analytical technique using one of a plurality of different functions to selectively vary the flow rate of the titrant and a sample. Significantly, Dasgupta does not teach or suggest a control technique that first employs a baseline value and then modifies the baseline value based on data obtained in conjunction with the baseline value. Such a technique recited by applicants' claim is distinctly different than varying a flow rate of the titrant and sample based on a predefined function, as is done by Dasgupta. Thus, Claim 35 is distinguishable over the combination of Bard and Dasgupta for this additional reason.

Claim 36 also depends from Claim 1, and also is therefore patentable for at least the same reason as Claim 1. Claim 36 recites that the controller is configured to use a baseline value for each reaction parameter to generate the desired product, to selectively vary each baseline value based on a linear function, and whenever a linear discontinuity is identified, to redefine the baseline value. Neither Bard nor Dasgupta teach or suggest a control technique including the function of redefining a baseline value whenever a linear discontinuity is identified. Thus, Claim 36 is distinguishable over the combination of Bard and Dasgupta for this additional reason.

Claim 37 is based on Claim 1 (before it was amended), and incorporates additional language further defining the dilution pumps. Specifically, Claim 37 recites a reaction system configured to produce the desired chemical product using at least two different reactants, and which includes a dilution pump for each reactant. The dilution pumps are configured to be coupled in fluid

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

communication with a corresponding reactant supply source and with the solvent supply source for a corresponding reactant, and to be logically coupled to the controller. Significantly, the dilution pumps are *operative to vary a concentration of a corresponding reactant using a solvent, such that the concentration of each reactant can be varied independently of the concentration of each other reactant.* Bard discloses a reaction system that includes two reactant supplies and a solvent supply. Bard specifically teaches that the solvent supply is not used to dilute either reactant. Instead, the solvent supply is used to flush the system and between different reactions. Even if one were to use the solvent supply disclosed by Bard to change the concentration of a reactant, because of the structural configuration disclosed by Bard, the solvent supply can only be used to vary the concentration of both reactants simultaneously. Bard's solvent supply is coupled in fluid communication with the mixing volume, and each reactant supply is also coupled in fluid communication with the mixing volume. If the solvent pump is not activated, then only the two reactants will flow into the mixing volume. If the solvent pump is activated, the solvent will also flow into the mixing volume, thereby changing the relative concentrations of each reactant by the same amount. Therefore, Bard's system is not configured to *independently* vary the concentration of each reactant using a solvent. Neither Bard, nor any other cited art, teaches or suggests that it would be desirable to modify Bard's system to enable the concentration of each reactant to be independently varied using a solvent. Dasgupta discloses that the concentration of a sample can be varied using a solvent; however, Dasgupta's titration system is not configured to vary the concentration of the titrant using a solvent (Dasgupta instead teaches changing a flow rate of the titrant using a pump). Thus, the suggested combination of Bard and Dasgupta cannot achieve an invention equivalent to applicants' claimed invention.

New Claim 38 recites a method for using a reaction system consistent with the elected claims to determine optimal reaction parameters. While Claim 38 may appear to be based on the non-elected claims, the Examiner had indicated that the non-elected method represent a different invention than those that have been elected, because the method originally claimed in the non-elected claims did not require the use of the dilution pumps recited in the elected claims. Claim 38 *does* include the dilution pump element recited in the elected claims, and therefore Claim 38 is consistent with the elected claims. Claim 38 distinguishes over the cited art because: (1) the combination of Bard and Dasgupta does not establish a *prima facie* case of obviousness, as discussed above; and

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600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314

(2) Claim 38 specifically recites the step of utilizing a dilution pump to vary a concentration of each reactant by adding a solvent to the reactant. As noted above, neither Bard nor Dasgupta teaches or suggests varying the concentration of each reactant by adding a solvent to that reactant, and thus, an artisan of ordinary skill would not be motivated to modify either reference to achieve applicants' claimed invention.

In view of the amendments to the title and the specification, and the Remarks set forth above, it will be apparent that the claims in this application define a novel and non-obvious invention, and that the application is in condition for allowance and should be passed to issue without further delay. Should any further questions remain, the Examiner is invited to telephone applicants' attorney at the number listed below.

Respectfully submitted,

Michael C. King
Registration No. 44,832

MCK/RMA:lrg

I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a sealed envelope as first class mail with postage thereon fully prepaid addressed to: Commissioner for Patents, Alexandria, VA 22313-1450, on May 23, 2005.

Date: May 23, 2005

LAW OFFICES OF RONALD M. ANDERSON
600 - 108th Avenue N.E., Suite 507
Bellevue, Washington 98004
Telephone: (425) 688-8816 Fax: (425) 646-6314